

FIGURE 1

A: BoNTA(H_c) synthetic gene (Version #1) SEQ ID NO: 1

GAATTCGAAACGatgCGTCTGCTGTCTACCTTCACTGAATACATCAAGAAC
ATCATCAATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGAT
CGACCTGTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACT
TCGATCCGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCC
AAAATCGAAGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACG
AAAACCTTCTCCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCC
ATCTCTCTGAACAATGAATACACCATCATCAACTGCATGGAAAAACAATT
CTGGTTGGAAAAGTATCTCTGAACCTACGGTGAAATCATCTGGACTCTGCAG
GACACTCAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGA
TCAACATCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAAC
AATCGTCTGAATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACC
AGAAACCGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATG
TTCAAACCTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATA
CTTCAATCTGTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTG
TACGACAACCAAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTA
CCTGCAGTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAAC
AAATACGTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGA
AAGGTCGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACCTTCC
CTGTACCGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACA
AGGACAATATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTT
AAGAACAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAG
AAAAGATCTTGTCTGCTCTGGAATCCCGGACGTTGGTAATCTGTCTCAG
GTAGTTGTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCA
AAATGAATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTT
CCACCAGTTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATC
GTCAGATCGAACGTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATC
CCGGTTGATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H_c) encoded protein (Version #1) SEQ ID NO: 2

MRLLSTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQI
QLFNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINCME
NNSGWKVSILNYGEIITLQDTQEIQRVVFKYSQMINISDYINRWIFVTITNN
RLNNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYIWIWIKYFNLF
DKELNEKEIKDLYDNQSNISGILKDFWGDYLYQYDKPYMLNLYDPNKYVDV
NNVGIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRN
NDRVYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKN
DQGITNKCKMNLQDNNNDIGFIGFHQFNNAIKLVASNWYNRQIERSRTL
GCSWEFIPVDDGWGERPL*

FIGURE 2

A: BoNTA(H_c) synthetic gene (version #2) SEQ ID NO: 3

GAATTCGAAACGatgTCTACCTTCACTGAATACATCAAGAACATCATCAAT
ACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCTGTC
TCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATCCGA
TCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAATCGA
AGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACGAAAACCTCT
CCACCTCCTTCTGGATCCGTATCCCGAAATACTTCAACTCCATCTCTCTG
AACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTGGA
AAGTATCTCTGAACCTACGGTGAAATCATCTGGACTCTGCAGGACACTCA
GGAAATCAAACAGCGTGTTGTATTCAAATACTCTCAGATGATCAACATCT
CTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGTCTG
AATAACTCCAAAATCTACATCAACGGCCGTCTGATCGACCAGAAACCGA
TCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAACCTG
GACGGTTGTCGTGACACTACCGCTACATCTGGATCAAATACTTCAATCT
GTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTGTACGACAA
CCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCAGT
ACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATACGT
TGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTCCG
CGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTACCG
TGGTACCAAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACAAT
ATCGTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAACAA
AGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGATC
TTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTTGT
AATGAAATCCAAGAACGACCAGGGTATCACTAACAATGCAAAATGAAT
CTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAGTT
CAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGATCG
AACGTTCCCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTGAT
GACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H_c) encoded protein (Version #2) SEQ ID NO: 4

MSTFTEYIKNIINTSILNLRYESNHLIDLTRYASKINIGSKVNFDPIDKNQIQLF
NLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTIINC MENNS
GWKVSLNYGEIWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTTITNNRLN
NSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHR YIWIKYFNLF DKE
LNEKEIKDL YDNQSN SGILKDFWGDYLYDKPY YMLNLYDPNKYVDVNNV
GIRGYMYLK GPRGSVMTTNIYLNSSLYRGTKFIKKYASGNKDNIVRNNDRV
YINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQGI
TNKCKMNLQDNNGNDIGFIGFHQFN NIAKLVASNWYNRQIERSSRTLGC SW
EFIPVDDGWGERPL*

FIGURE 3

A: BoNTA(H_c) synthetic gene (Version #3) SEQ ID NO: 5

GAATTCGAAACGatgGCCTCTACCTTCACTGAATACATCAAGAACATCATC
AATACCTCCATCCTGAACCTGCGCTACGAATCCAATCACCTGATCGACCT
GTCTCGCTACGCTTCCAAAATCAACATCGGTTCTAAAGTTAACTTCGATC
CGATCGACAAGAATCAGATCCAGCTGTTCAATCTGGAATCTTCCAAAAT
CGAAGTTATCCTGAAGAATGCTATCGTATACAACCTCTATGTACGAAAACCT
TCTCCACCTCCTTCTGGATCCGATCCCGAAATACTTCAACTCCATCTCTC
TGAACAATGAATACACCATCATCAACTGCATGGAAAACAATTCTGGTTG
GAAAGTATCTCTGAACTACGGTGAAATCATCTGGACTCTGCAGGACACT
CAGGAAATCAAACAGCGTGTGTATTCAAATACTCTCAGATGATCAACA
TCTCTGACTACATCAATCGCTGGATCTTCGTTACCATCACCAACAATCGT
CTGAATAACTCCAAAATCTACATCAACGCCGCTCTGATCGACCAGAAAC
CGATCTCCAATCTGGGTAACATCCACGCTTCTAATAACATCATGTTCAAA
CTGGACGGTTGTCGTGACACTCACCGCTACATCTGGATCAAATACTTCAA
TCTGTTTCGACAAAGAACTGAACGAAAAAGAAATCAAAGACCTGTACGAC
AACCAGTCCAATTCTGGTATCCTGAAAGACTTCTGGGGTGACTACCTGCA
GTACGACAAACCGTACTACATGCTGAATCTGTACGATCCGAACAAATAC
GTTGACGTCAACAATGTAGGTATCCGCGGTTACATGTACCTGAAAGGTC
CGCGTGGTTCTGTTATGACTACCAACATCTACCTGAACTCTTCCCTGTAC
CGTGGTACCAAATTCATCATCAAGAAATACGCGTCTGGTAACAAGGACA
ATATCGTTTCGCAACAATGATCGTGTATACATCAATGTTGTAGTTAAGAAC
AAAGAATACCGTCTGGCTACCAATGCTTCTCAGGCTGGTGTAGAAAAGA
TCTTGTCTGCTCTGGAAATCCCGGACGTTGGTAATCTGTCTCAGGTAGTT
GTAATGAAATCCAAGAACGACCAGGGTATCACTAACAAATGCAAAATGA
ATCTGCAGGACAACAATGGTAACGATATCGGTTTCATCGGTTTCCACCAG
TTCAACAATATCGCTAAACTGGTTGCTTCCAACCTGGTACAATCGTCAGAT
CGAACGTTTCTCTCGCACTCTGGGTTGCTCTTGGGAGTTCATCCCGGTTG
ATGACGGTTGGGGTGAACGTCCGCTGtaaGAATTC

B: BoNTA(H_c) encoded protein (Version #3) SEQ ID NO: 6

MASTFTEYIKNIINTSILNLRYESNHLIDLSRYASKINIGSKVNFDPIDKNQIQL
FNLESSKIEVILKNAIVYNSMYENFSTSFWIRIPKYFNSISLNNEYTHINCMENN
SGWKVSLNYGEIHWTLQDTQEIKQRVVFKYSQMINISDYINRWIFVTITNNRL
NNSKIYINGRLIDQKPISNLGNIHASNNIMFKLDGCRDTHRYTIWIKYFNLFDK
ELNEKEIKDLYDNQSNISGILKDFWGDYLYQYDKPYMLNLYDPNKYVDVNN
VGIRGYMYLKGPRGSVMTTNIYLNSSLYRGTKFIIKKYASGNKDNIVRNDR
VYINVVVKNKEYRLATNASQAGVEKILSALEIPDVGNLSQVVVMKSKNDQ
GITNKCKMNLQDNNGNDIGFIGFHQFNIAKLVASNWNRYNIERSRSLGCS
WEFIPVDDGWGERPL*

FIGURE 4

A: BoNTB(H_c) synthetic gene SEQ ID NO: 7

GAATTCACGatgGCCAACAAATACAATTCCGAAATCCTGAACAATATCAT
CCTGAACCTGCGTTACAAAGACAACAATCTGATCGATCTGTCTGGTTACG
GTGCTAAAGTTGAAGTATACGACGGTGTGAACTGAATGACAAGAACCA
GTTCAAACCTGACCTCTTCCGCTAACTCTAAGATCCGTGTTACTCAGAATC
AGAACATCATCTTCAACTCCGTATTCCTGGACTTCTCTGTTTCCTTCTGGA
TTCGTATCCCGAAATACAAGAACGACGGTATCCAGAATTACATCCACAA
TGAATACACCATCATCAACTGCATGAAGAATAACTCTGGTTGGAAGATC
TCCATCCGCGGTAAACCGTATCATCTGGACTCTGATCGATATCAACGGTAA
GACCAAATCTGTATTCTTCGAATACAACATCCGTGAAGACATCTCTGAAT
ACATCAATCGCTGGTTCTTCGTTACCATCACCAATAACCTGAACAATGCT
AAAATCTACATCAACGGTAAACTGGAATCTAATACCGACATCAAAGACA
TCCGTGAAGTTATCGCTAACGGTGAAATCATCTTCAAACCTGGACGGTGA
CATCGATCGTACCCAGTTCATCTGGATGAAATACTTCTCCATCTTCAACA
CCGAAGTGTCTCAGTCCAATATCGAAGAACGGTACAAGATCCAGTCTTA
CTCCGAATACCTGAAAGACTTCTGGGGTAATCCGCTGATGTACAACAAA
GAATACTATATGTTCAATGCTGGTAACAAGAAGTCTTACATCAAAGTGA
AGAAAGACTCTCCGGTTGGTGAAATCCTGACTCGTTCCAAATACAACCA
GAACTCTAAATACATCAACTACCGCGACCTGTACATCGGTGAAAAGTTC
ATCATCCGTCGCAAATCTAACTCTCAGTCCATCAATGATGACATCGTACG
TAAAGAAGACTACATCTACCTGGACTTCTTCAACCTGAATCAGGAATGG
CGTGTATACACCTACAAGTACTTCAAGAAAGAAGAAGAAAAGCTTTTCC
TGGCTCCGATCTCTGATTCCGACGAACTCTACAACACCATCCAGATCAAA
GAATACGACGAACAGCCGACCTACTCTTGCCAGCTGCTGTTCAAGAAAG
ATGAAGAATCTACTGACGAAATCGGTCTGATCGGTATCCACCGTTTCTAC
GAATCTGGTATCGTATTCTGAAGAATACAAAGACTACTTCTGCATCTCCAA
ATGGTACCTGAAGGAAGTTAAACGCAAACCGTACAACCTGAAACTGGGT
TGCAATTGGCAGTTCATCCCGAAAGACGAAGGTTGGACCGAAtagtaaGAA
TTC

B: BoNTB(H_c) encoded protein SEQ ID NO: 8

MANKYNSEILNNIILNRLRYKDNNDLDSGYGAKVEVYDGVELNDKNQFKLT
SSANSKIRVTQNQNIIFNSVFLDFSVSFWIRIPKYKNDGIQNYIHNEYTIINCM
KNNSGWKISIRGNRIIWTLLIDINGKTKSVFFEYNIREDISSEYINRWFFVTITNNL
NNAKIYINGKLESNTDIKDIREVIANGEIIFKLDGDDIDRTQFIWMKYFSIFNTEL
SQSNIEERYKIQSYSEYKDFWGNPLMYNKEYYMFNAGNKNKYIKLKKDSP
VGEILTRSKYNQNSKYINYRDLYIGEFIRRKSNSSQINDDIVRKEDYIYLDLF
FNLNQEWVRVYTYKYFKKEEEKLFLAPISDSDELNTIQIKEYDEQPTYSCQL
LFFKDEESTDEIGLIGIHRFYESGIVFEEYKDYFCISKWYLKEVKRKPYNLKL
GCNWQFIPKDEGWTE**

FIGURE 5

A: BoNTC₁(H_c) synthetic gene SEQ ID NO: 9

GAATTACGatgACCATCCCATTCAACATCTTCTCCTACACCAACAACTCC
CTGTTGAAGGACATCATCAACGAGTACTTCAACAACATCAACGACTCCA
AGATCCTGTCCCTGCAGAACCGTAAGAACACCTTGGTCGACACCTCCGG
TTACAACGCCGAGGTCTCCGAGGAGGGTGACGTCCAGCTGAACCCAATC
TTCCCATTTCGACTTCAAGCTGGGTTCTCCTCCGGTGAGGACAGAGGTAAGGT
CATCGTCACCCAGAACGAGAACATCGTCTACAACCTCCATGTACGAGTCC
TTCTCCATCTCCTTCTGGATCAGAATCAACAAGTGGGTCTCCAACCTGCC
AGGTTACACCATCATCGACTCCGTCAAGAACAACCTCCGGTTGGTCCATCG
GTATCATCTCCAACCTTCTGGTCTTCAACCTGAAGCAGAACGAGGACTCC
GAGCAGTCCATCAACTTCTCCTACGACATCTCCAACAACGCTCCTGGTTA
CAACAAGTGGTTCTTCGTCACCGTCACCAACAACATGATGGGTAACATG
AAGATCTACATCAACGGTAAGCTGATCGACACCATCAAGGTCAAGGAGT
TGACCGGTATCAACTTCTCCAAGACCATCACCTTCGAGATCAACAAGATC
CCAGACACCGGTCTGATCACCTCCGACTCCGACAACATCAACATGTGGA
TCCGTGACTTCTACATCTTCGCCAAGGAGTTGGACGGTAAGGACATCAA
CATCCTGTTCAACTCCTTGCAGTACACCAACGTCGTCAAGGACTACTGGG
GTAACGACCTGAGATACAACAAGGAGTACTACATGGTCAACATCGACTA
CTTGAACAGATACATGTACGCCAACTCCAGACAGATCGTCTTCAACACC
AGACGTAACAACAACGACTTCAACGAGGGTTACAAGATCATCATCAAGC
GTATCAGAGGTAACACCAACGACACCAGAGTCAGAGGTGGTGACATCCT
GTACTTCGACATGACTATCAACAACAAGGCCTACAACCTGTTTCATGAAG
AACGAGACCATGTACGCCGACAACCACTCCACCGAGGACATCTACGCCA
TCGGTCTGCGTGAGCAGACCAAGGACATCAACGACAACATCATCTTCCA
GATCCAGCCAATGAACAACACTTACTACTACGCTTCCCAGATCTTCAAGT
CCAACCTTCAACGGTGAGAACATCTCCGGTATCTGTTCCATCGGTACCTAC
AGATTCCGTCTGGGTGGTGACTGGTACAGACACAACCTACTTGGTTCCAAC
TGTC AAGCAGGGTAAC TACGCCTCCTTGCTGGAGTCCACTTCCACCCACT
GGGGATTTCGTCCCAGTCTCCGAGGtaatagGAATTC

B: BoNTC₁(H_c) encoded protein SEQ ID NO: 10

MTIPFNIFS YTNNSLLKDIINEYFNNINDSKILSLQNRKNTLVDTSGYNAEVSE
EGDVQLNPIFPDFKLGSSGEDRGKVIVTQENENIVYNSMYESFSISFWIRINK
WVSNLPGYTIIDSVKNNSGWSIGIISNFLVFTLKQNEDEQSINFSYDISNNAP
GYNKWFFVTVTNNMMGMNMIYINGKLIDTIKVKELTGINFSTITFEINKIPD
TGLITSDSDNINMWIRDFYIFAKELDGKDINILFNSLQYTNVVKDYWGNDLR
YNKEYYMNIDYLNRYMYANSRQIVFNTRNNNDFNEGYKIIKRIRGNTN
DTRVRGGDILYFDMTINNKAYNLFMKNETMYADNHSTEDIYAIGLREQTKD
INDNIIFQIQPMNNTY Y Y ASQIFKSNFNGENISGICSIGTYRFRLLGGDWYRHN
YLVPTVKQGN YASLLESTSTHWGFVPVSE**

FIGURE 6

A: BoNTD(H_c) synthetic gene SEQ ID NO: 11

GAATTCACGatgCGTTTGAAGGCTAAGGTCAACGAGTCCTTCGAGAACAC
CATGCCATTCAACATCTTCTCCTACACCAACAACCTCCTTGTTGAAGGACA
TCATCAACGAGTACTTCAACTCCATCAACGACTCCAAGATCTTGTCTTGG
CAGAACAAGAAGAACGCCTTGGTCGACACCTCCGGTTACAACGCCGAGG
TCAGAGTCGGTGACAACGTCCAGTTGAACACCATCTACACCAACGACTT
CAAGTTGTCCTCTTCCGGTGACAAGATCATCGTCAACTTGAACAACAACA
TCTTGTACTCCGCCATCTACGAGAACTCCTCTGTCTCCTTCTGGATCAAG
ATCTCCAAGGACTTGACCAACTCCCACAACGAGTACACCATCATCAACT
CCATCGAGCAGAACTCCGGTTGGAAGTTGTGTATCCGTAACGGTAACAT
CGAGTGGATCTTGCAGGACGTCAACCGTAAGTACAAGTCCTTGATCTTCG
ACTACTCCGAGTCCTTGTCCACACCGGTTACACCAACAAGTGGTTCCTTC
GTCACCATCACCAACAACATCATGGGTTACATGAAGTTGTACATCAACG
GTGAGTTGAAGCAGTCCCAGAAGATCGAGGACCTGGACGAGGTCAAGCT
GGACAAGACCATCGTCTTCGGTATCGACGAGAACATCGACGAGAACCAG
ATGTTGTGGATCCGTGACTTCAACATCTTCTCCAAGGAGCTGTCCAACGA
GGACATCAACATCGTCTACGAGGGTTCAGATCCTGAGGAACGTCATCAAG
GACTACTGGGGTAACCCACTGAAGTTCGACACCGAGTACTACATCATCA
ACGACAACATACATCGACCGTTACATCGCCCCAGAGTCCAACGTCCTGGT
CCTGGTCCAGTACCCTGACCGTTCCAAGCTGTACACCGGTAACCTATCA
CCATCAAGTCCGTCTCCGACAAGAACCCTTACTCCCGTATCCTGAACGGT
GACAACATCATCCTGCACATGCTGTACAACCTCCCGTAAGTACATGATCAT
CCGTGACACCGACACCATCTACGCCACCCAGGGTGGTGACTGTTCCAG
AACTGTGTCTACGCCCTGAAGCTGCAGTCCAACCTGGGTAACTACGGTAT
CGGTATCTTCTCCATCAAGAACATCGTCTCCAAGAACAAGTACTGCTCCC
AGATCTTCTCCTCCTTCCGTGAGAACACCATGCTGCTGGCCGACATCTAC
AAGCCTTGGCGTTTCTCCTTCAAGAACGCCTACACTCCTGTGCGCCGTCAC
CAACTACGAGACCAAGCTGCTGTCCACCTCCTCCTTCTGGAAGTTCATCT
CCCGTGACCCAGGTTGGGTCGAGtaatagGAATTC

B: BoNTD(H_c) encoded protein SEQ ID NO: 12

MRLKAKVNESFENTMPFNIFS YTNNSLLKDIINEYFNSINDSKILSLQNKKNA
LVDTSGYNAEVRVGDNVQLNTIYTNDFKLSSSGDKIIVNLNNNILYSAIYENS
SVSFWIKISKDLTNSHNEYTIINSIEQNSGWKLCIRNGNIEWILQDVNRKYKS
LIFDYSESLSHTGYTNKWWFVTITNNIMGYMKLYINGELKQSQKIEDLDEVK
LDKTIVFGIDENIDENQMLWIRDFNIPFSKELSNEDINIVYEGQILRNVIKDYW
GNPLKFDTEYYIINDNYIDRYIAPESNVLVLVQYPDRSKLYTGNPITIKSVSD
KNPYSRILNGDNILHMLYNSRKYMIIRDTDIYATQGGDCSQNCVYALKLQ
SNLGNYGIGIFSINKNIVSKNKYCSQIFSSFRENTMLLADIYKPWRFSFKNAYTP
VAVTNYETKLLSTSSFWKFISRDPGWVE**

FIGURE 7

A: BoNTE(H_c) synthetic gene SEQ ID NO: 13

GAATTCACCCatgGGAGAGAGTCAGCAAGAACTAAATTCTATGGTAACTGA
TACCCTAAATAATAGTATTCCTTTTAAGCTTTCTTCTTATACAGATGATAA
AATTTTAATTTCTACTTCAACAAGTTCTTCAAGAGAATTAAGTCTTCTTC
CGTTTTAAACATGAGATACAAGAATGATAAATACGTCGACACTTCCGGT
TACGACTCCAATATCAACATTAACGGTGACGTGTACAAGTACCCAACATA
ACAAAAACCAATTCGGTATCTACAACGACAAGCTTACTGAGCTGAACAT
CTCTCAAAACGACTACATTATCTACGACAACAAGTACAAGAACTTCTCTA
TTTCTTTCTGGGTGAGGATTCCTAACTACGACAACAAGATCGTCAACGTT
AACAACGAGTACACTATCATCAACTGTATGAGAGACAACAACCTCCGGTT
GGAAGGTCTCTCTTAACCACAACGAGATCATTGACCTTGCAAGACAA
CGCAGGTATTAACCAAAAGTTAGCATTCAACTACGGTAACGCAAACGGT
ATTTCTGACTACATCAACAAGTGGATTTTCGTCACTATCACTAACGACAG
ATTAGGTGACTCTAAGCTTTACATTAACGGTAACTTAATCGACCAAAAGT
CCATTTTAAACTTAGGTAACATTCACGTTTCTGACAACATCTTATTCAAG
ATCGTTAACTGCAGTTACACCAGATACATTGGCATTAGATACTTCAACAT
TTTCGACAAGGAGTTAGACGAGACCGAGATTCAAACCTTTATACAGCAAC
GAACCTAACACCAATATTTTGAAGGACTTCTGGGGTAACTACTTGCTTTA
CGACAAGGAATACTACTTATTAACCGTGTAAAGCCAAACAACCTTCATT
GATAGGAGAAAGGATTCTACTTTAAGCATTAAACAACATCAGAAGCACTA
TTCTTTTAGCTAACAGATTATACTCTGGTATCAAGGTTAAGATCCAAAGA
GTTAACAACCTCTTCTACTAACGATAACCTTGTTAGAAAGAACGATCAGGT
CTATATTAACCTTCGTCGCTAGCAAGACTCACTTATTCCCATTATATGCTG
ATACCGCTACCACCAACAAGGAGAAGACCATCAAGATCTCCTCCTCTGG
CAACAGATTTAAACCAAGTCGTCGTTATGAACTCCGTCGGTAACAACCTGTA
CCATGAACTTTAAAAATAATAATGGAAATAATATTGGGTTGTTAGGTTTC
AAGGCAGATACTGTAGTTGCTAGTACTTGGTATTATACCCACATGAGAG
ATCACACCAACAGCAATGGATGTTTTTGGAACTTTATTTCTGAAGAACAT
GGATGGCAAGAAAAAataa
TagGGATCC GCGGCCGC ACGCGT CCCGGG ACTAGT GAATTC

B: BoNTE(H_c) encoded protein SEQ ID NO: 14

MGESQQELNSMVTDTLNNIPFKLSSYTDDKILISYFNKFFKRIKSSSVLNMR
YKNDKYVDTSYDSNININGDVYKYPTNKNQFGIYNDKLTENISQNDYIIY
DNKYKNFSISFWVRIPNYDNKIVNVNNEYTIINCMRDNNSGWKVS LNHNELI
WTLQDNAGINQKLA FN YGNANGISDYINKWIFVTITNDR LGDSKLYINGNLI
DQKSILNLGNIHVSDNLFKIVNCSYTRYIGIRYFNIFDKELDETEIQTLYSNEP
NTNILKDFWGNLYLLYDKEYYLLNVLPNNFIDRRKDSTLSINNIRSTILLANR
LYSGIKVKIQRVNNSSTNDNLVRKNDQVYINFVASKTHLFLPLYADTATTNKE
KTIKISSSGNRFNQVVMNSVGNNTMNFKNNGNNGNIGLLGFKADTVVAST
WYYTHMRDHTNSNGCFWNFISEEHGWQEK**

Enclume 1

100220" 58707660

AMINO ACID AND DESIGNED NUCLEOTIDE SEQUENCE OF BONTE(Hc)

Asu II

TTC GAA ACG ATG ATT TTA ATT TCC TAC TTC AAC AAG TTC TTC AAG AGA ATT AAG TCT TCC GTT TTA AAC ATG AGA TAC AAG AAT GAT AAA TAC GTC
M I L I S Y F N K F F K R I K S S V L N M R Y K N D K Y V
GAC ACT TCC GGT TAC GAC TCC AAT ATC AAC ATT AAC GGT GAC GTG TAC AAG TAC CCA ACT AAC AAA AAC CAA TTC GGT ATC TAC AAC GAC AAG CTT ACT GAG CTG
D T S G Y D S N I N I N G D V Y K Y P T N K N Q F G I Y N D K L (1) E L
AAC ATC TCT CAA AAC GAC TAC ATT ATC TAC GAC AAC AAG TAC AAC TCC GGT TGG AAG GTC TCT CTT AAC CAC AAC GAG ATC ATT TGG ACC TTG CAA GAC AAC GCA GGT
N I S Q N D Y I I Y D N K Y K N F S I S F W V R I P N Y D N K I V N V
AAC AAC GAG TAC ACT ATC AAC TGT ATG AGA GAC AAC AAC TCC GGT TGG AAG GTC TCT CTT AAC CAC AAC GAG ATC ATT TGG ACC TTG CAA GAC AAC GCA GGT
N N E Y T I I N C M R D N N S G W K V S L N H N E I I W (T) L Q D N A G
ATT AAC CAA AAG TTA GCA TTC AAC TAC GGT AAC GCA AAC GGT ATT TTA AAC TTA GGT AAC ATT CAC GTT TCT GAC AAC ATC TTA TTC AAG ATC GTT AAC TGC AGT TAC
I N Q K L A F N Y G N A N G I S D Y I N K W I F V T I T N D R L G D S
AAG CTT TAC ATT AAC GGT AAC TTA ATC GAC CAA AAG TCC ATT TTA AAC TTA GGT AAC ATT CAC GTT TCT GAC AAC ATC TTA TTC AAG ATC GTT AAC TGC AGT TAC
K L Y I N G N L I D Q K S I L N L G N I H V S D N I L F K I V N C S Y
ACC AGA TAC ATT GGC ATT AGA TAC TTC AAC ATT TTC GAC AAG GAG TTA GAC GAG AOC GAG ATT CAA ACT TTA TAC AGC AAC GAA CCT AAC ACC AAT ATT TTG AAG
T R Y I G I R Y F N I F D K E L D E T E I Q T L Y S N E P N T N I L K
GAC TTC TGG GGT AAC TAC TTG CTT TAC GAC AAG GAA TAC TAC TTA TTA AAC GTG TTA AAG CCA AAC AAC TTC ATT GAT AGG AGA AAG GAT TCT ACT AAC GAT AAC CTT GTT AGA
D F W G N Y L Y D K E Y Y L L N V L K P N N F I D R R K D S T L S I
AAC AAC ATC AGA AGC ACT ATT CTT TTA GCT AAC AGA TTA TAC TCT GGT ATC AAG GTT AAG ATC CAA AGA GTT AAC AAC TCT TCT ACT AAC GAT AAC CTT GTT AGA
N N I R S T I L L A N R L Y S G I K V K I Q R V N N S S T N D N L V R
AAG AAC GAT CAG GTC TAT ATT AAC TTC GTC GGT AOC AAC ACT CAC TTA TTC CCA TTA TAT GGT GAT ACC GGT AOC AAC AAG GAG AAG ACC ATC AAG ATC TCC
K N D Q V Y I N F V A S K T H L F P L Y A D T A T T N K E K T I K I S
TCC TCT GGC AAC AGA TTT AAC CAA GTC GTC GTC ATT ATG AAC TCC GTC GGT AAC TGT ACC ATG AAC TTT AAA AAT AAT AAT GGA AAT AAT ATT GGG TTG TTA GGT
S S G N R F N Q V V M N S V G N N C T M N F K N N N G N N I G L L G
TTC AAG GCA GAT ACT GTA GTT GGT ACT TGG TAT TAT ACC CAC ATG AGA GAT CAC ACC AAC AGC AAT GGA TGT TTT TGG AAC TTT ATT TCT GAA GAA CAT GGA
F K A D T V V A S
TGG CAA GAA AAA TAA TAG GGA TCC
W Q E K ter BamHI

Fig 8

FIGURE 9

A: BoNTF(H_c) synthetic gene SEQ ID NO: 15

GAATTCACGatgTCCTACACCAACGACAAGATCCTGATCTTGTACTTCAAC
AAGCTGTACAAGAAGATCAAGGACAACCTCCATCTTGGACATGAGATACG
AAAACAATAAGTTCATCGACATCTCCGGTTACGGTTCCAACATCTCCATC
AACGGTGACGTCTACATCTACTCCACCAATAGAAACCAGTTCGGAATCT
ACTCCTCCAAGCCTTCCGAGGTCAACATCGCTCAGAACAACGACATCAT
CTACAACGGAAGATACCAGAACTTCTCCATCTCCTTCTGGGTCCGTATCC
CAAAGTACTTCAACAAGGTCAACCTGAATAACGAGTACACCATCATCGA
CTGCATCCGTAACAATAACTCCGGATGGAAGATCTCCCTGAACTACAAC
AAGATCATCTGGACCCTGCAGGACACCGCCGGTAACAATCAGAAGTTGG
TCTTCAACTACACCCAGATGATCTCCATCTCCGACTACATCAACAAGTGG
ATCTTCGTCACCATCACCAATAACCGTTTGGGAAACTCCAGAATCTACAT
CAACGGTAACTTGATCGACGAGAAGTCCATCTCCAACCTGGGTGACATC
CACGTCTCCGACAACATTTTGTTC AAGATCGTCGGTTGTAACGACACCCG
TTACGTCGGGATCCGTTACTTCAAAGTCTTCGACACTGAGTTGGGTAAAG
CCGAGATCGAGACCTTGTACTCCGACGAGCCTGACCCATCCATCCTGAA
GGACTTCTGGGGTAACTACCTGCTGTACAACAAACGTTACTACTTGCTGA
ACTTGTTGCGTACCGACAAGTCCATCACCCAGAACTCCAACCTTCTGAAC
ATCAACCAGCAGAGAGGTGTCTACCAGAAGCCAAACATCTTCTCCAACA
CCAGATTGTACACCGGAGTCGAGGTCATTATCAGAAAGAACGGATCTAC
TGATATTTCCAACACCGATAACTTCGTCAGAAAGAACGATCTGGCTTACA
TCAACGTTGTGACAGAGATGTGCAATACCGTCTGTACGCCGATATCTCT
ATCGCCAAACCTGAAAAGATCATCAAGCTGATCCGTACCTCTAACTCTA
ACAACTCTCTGGGACAAATCATCGTCATGGACTCCATCGGTAATAACTGT
ACCATGAACTTCCAGAACAACAACGGTGGAACATCGGTTTGTGGGTT
TCCACTCCAACAACCTTGGTCGCTTCTCTCTGGTACTACAACAACATCCGT
AAGAACACCTCCTCCAACGGTTGCTTCTGGTCCTTCATCTCCAAGGAGCA
CGGTTGGCAGGAGAACTaatagGAATTC

B: BoNTF(H_c) encoded protein SEQ ID NO: 16

MSYTNDKILILYFNKL YKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY
STNRNQFGIYSSKPSSEVNIAQNNDIYNGRYQNFSISFWVRIPKYFNKVNLLN
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNYSQMISISDYIN
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNLFKIVGCNDTRYV
GIRYFKVFDTELKTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLIRTSNSNNSLQIIVMDSI
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYYNNIRKNTSSNGCFWSFIS
KEHGWQEN**

FIGURE 10

A: BoNTG(H_c) synthetic gene SEQ ID NO: 17

GAATTCACGatgAAGGACACCATCCTGATCCAGGTCTTCAACAACACTACATC
TCCAACATCTCCTCCAACGCCATCCTGTCCCTGTCCTACCGTGGTGGTCG
TCTGATCGACTCCTCCGGTTACGGAGCCACCATGAACGTCGGTTCCGACG
TCATCTTCAACGACATCGGTAACGGTCAGTTCAAGCTGAACAACCTCCGA
GAACTCCAACATCACCGCCCACCAGTCCAAGTTCGTCTGTCTACGACTCCA
TGTTTCGACAACCTTCTCCATCAACTTCTGGGTCCGTACCCCAAAGTACAAC
AACAACGACATCCAGACCTACCTGCAGAACGAGTACACCATCATCTCCT
GTATCAAGAACGACTCCGGTTGGAAGGTCTCCATCAAGGGAAACCGTAT
CATCTGGACCCTGATCGACGTCAACGCCAAGTCCAAGTCCATCTTCTTCG
AGTACTCCATCAAGGACAACATCTCCGACTACATCAACAAGTGGTTCTCC
ATCACCATCACCAACGACCGTCTGGGTAACGCCAACATCTACATCAACG
GTTCCCTGAAGAAGTCCGAGAAGATCCTGAACCTGGACCGTATCAACTC
CTCCAACGACATCGACTTCAAGCTGATCAACTGTACCGACACCACCAAG
TTCGTCTGGATCAAGGACTTCAACATCTTCGGTCGTGAGCTGAACGCCAC
CGAGGTCTCCTCCCTGTACTGGATCCAGTCCTCCACCAACACCCTGAAGG
ACTTCTGGGGAAACCCACTGCGTTACGACACCCAGTACTACCTGTTCAAC
CAGGGTATGCAGAACATCTACATCAAGTACTTCTCCAAGGCCTCCATGG
GTGAGACCGCCCCTCGTACCAACTTCAACAACGCCGCCATCAACTACCA
GAACCTGTACCTGGGTCTGCGTTTCATCATCAAGAAGGCCTCCAACCTCCC
GTAACATCAACAACGACAACATCGTCCGTGAGGGTGACTACATCTACCT
GAACATCGACAACATCTCCGACGAGTCTACCGTGTCTACGTCCTGGTCA
ACTCCAAGGAGATCCAGACCCAGCTGTTCTTGCCCCAATCAACGACGA
CCCTACCTTCTACGACGTCTGCGAGATCAAGAAGTACTACGAGAAGACC
ACCTACAACCTGTCAGATCCTGTGCGAGAAGGACACCAAGACCTTCGGAC
TGTTCCGTATCGGTAAGTTCGTCAAGGACTACGGTTACGTCTGGGACACC
TACGACAACCTACTTCTGTATCTCCAGTGGTACCTGCGTCGTATCTCCGA
GAACATCAACAAGCTGCGTCTGGGATGTAAGTGGCAGTTCATCCCAGTC
GACGAGGGTTGGACCGAGGtaaatagGAATTC

B: BoNTG(H_c) encoded protein SEQ ID NO: 18

MKDTILIQVFNNYISNISSNAILSLSYRGGRLIDSSGYGATMNVGSDVIFNDIG
NGQFKLNSENSENITAHQSKFVVYDSMFDNFSINFWVRTPKYNNNDIQTYL
QNEYTIISCIKND SGWKVSIKGNRIIWLIDVNAKSKSIFFEYSIKDNISDYINK
WFSITITNDR LGNANIYINGSLKKSEKILNLD RINSSNDIDFKLINCTD TTKFV
WIKDFNIFGRELNATEVSSLYWIQSSTNTLKDFWGNPLRYDTQYYLFNQGM
QNIYIKYFSKASMGETAPRTNFNNAAINYQNL YLGLRFIIKKASNSRNINNDN
IVREGDYIYLNIDNISDES YRVYVLVNSKEIQTQLFLAPINDDPTFYDVLQIKK
YYEKT TYNCQILCEKDTKTFGLFGIGKFVKDYGYVWD TYDNYFCISQWYLR
RISENINKLRLG CNWQFIPVDEGWTE**

FIGURE 11

A: BoNTA(H_N) synthetic gene SEQ ID NO: 19

atgGCTCTGAACGACCTGTGCATCAAAGTTAACAACCTGGGACCTGTTCTTC
TCCCCGTCTGAAGACAACCTTCACTAACGACCTGAACAAAGGCGAAGAAA
TCACCTCCGACACTAACATCGAAGCTGCTGAAGAAAACATCTCTCTGGA
CCTGATCCAGCAGTACTACCTGACTTTCAACTTCGACAACGAACCGGAA
AACATCTCCATCGAAAACCTGTCTTCCGACATCATCGGTGAGCTGGAAC
GATGCCGAACATCGAACGCTTCCCGAACGGCAAGAAATACGAACTGGAC
AAATACACCATGTTCCACTACCTGCGTGCTCAGGAATTTCGAACACGGTA
AATCTCGTATCGCTCTGACTAACTCCGTTAACGAAGCTCTGCTGAACCCG
TCTCGCGTTTACACCTTCTTCTTCCGACTACGTTAAGAAAGTTAACAA
AGCTACTGAAGCTGCTATGTTTCTGGGTTGGGTTGAACAGCTGGTTTACG
ACTTCACCGACGAAACTTCTGAAGTTTCCACCACTGACAAAATCGCTGAC
ATCACTATCATCATCCCGTACATCGGCCCGGCTCTGAACATCGGTAACAT
GCTGTACAAAGACGACTTCGTTGGTGCTCTGATCTTCTCTGGCGCTGTTA
TCCTGCTGGAATTCATCCCGGAAATCGCTATCCCGGTTCTGGGTACCTTC
GCTCTGGTTTCTTACATCGCTAACAAAGTTCTGACTGTTTACAGCCATCGA
CAACGCTCTGTCTAAACGTAACGAAAAATGGGACGAAGTTTACAAATAC
ATCGTTACTAACTGGCTGGCTAAAGTTAACTCAGATCGACCTGATCCG
TAAGAAGATGAAAGAAGCTCTGGAAAACAGGCTGAAGCTACTAAAGC
TATCATCAACTACCAGTACAACCAGTACACCGAAGAAGAAAAGAACAAC
ATCAACTTCAACATCGATGACCTGTCTCTAAACTGAACGAATCCATCAA
CAAAGCTATGATCAACATCAACAAATTCCTGAACCAAGTCTGTTTCTCT
ACCTGATGAACTCTATGATCCCGTACGGCGTTAAACGCCTGGAAGACTTC
GACGCTTCCCTGAAAGACGCTCTGCTGAAATACATCCGTGACAACTACG
GTACTCTGATCGGCCAGGTTGACCGTCTGAAAGACAAGGTTAACAAACAC
CCTGTCTACTGACATCCCGTTCCAGCTGTCCAAATACGTTGACAACCAAGta
a

B: BoNTA(H_N) encoded protein SEQ ID NO: 20

MALNDLCIKVNNWDLFFSPSEDNFTNDLNKGEEITSDTNIEAAEENISLDLIQ
QYYLTFNFDNEPENISIENLSSDIIGQLELMPNIEFPNGKKYELDKYTMFHY
LRAQEFEHGKSRIALTNSVNEALLNPSRVYTFSSDYVKKVKNKATEAAMFL
GWVEQLVYDFTDETSEVSTTDKIADITIIPYIGPALNIGNMLYKDDFVGALIF
SGAVILLEFIPEIAIPVLGTFALVSYIANKVLTQVQIDNALSKEKRWDEVYK
YIVTNWLAKVNTQIDLIRKKMKEALENQAEATKAIIYQYNQYTEEEKNNI
NFNIDDLSSKLNESINKAMININKFLNQCSVSYLMNSMIPYGVKRLEDFDASL
KDALLKYIRDNYGTLIGQVDRLKDKVNNTLSTDIPFQLSKYVDNQ*

FIGURE 12

A: BoNTB(H_N) synthetic gene SEQ ID NO: 21

atgGCTCCAGGAATCTGTATCGACGTCGACAACGAGGACTTGTTCCTTCATC
GCTGACAAGAACTCCTTCTCCGACGACTTGTCCAAGAACGAGAGAATCG
AGTACAACACCCAGTCCAACCTACATCGAGAACGACTTCCCAATCAACGA
GTTGATCTTGGACACCGACTTGATCTCCAAGATCGAGTTGCCATCCGAGA
ACACCGAGTCCTTGACTGACTTCAACGTCGACGTCCCAGTCTACGAGAA
GCAACCAGCTATCAAGAAGATTTTCACCGACGAGAACACCATCTTCCAA
TACCTGTACTCTCAGACCTTCCCTTTGGACATCAGAGACATCTCCTTGAC
CTCTTCCCTTCGACGACGCCCTGCTGTTCTCCAACAAGGTCTACTCCTTCTT
CTCCATGGACTACATCAAGACTGCTAACAAGGTCGTCGAGGCCGGTTTG
TTCGCTGGTTGGGTCAAGCAGATCGTCAACGATTTTCGTCATCGAGGCTAA
CAAGTCCAACACCATGGACAAGATTGCCGACATCTCCTTGATTGTCCCAT
ACATCGGTTTGGCCTTGAACGTCGGTAACGAGACCGCCAAGGGTAACTT
CGAGAACGCTTTCGAGATCGCTGGTGCCTCCATCTTGTTGGAGTTCATCC
CAGAGTTGTTGATCCCAGTCGTCGGTGCCTTCTTGTTGGAGTCCACATC
GACAACAAGAACAAGATCATCAAGACCATCGACAACGCTTTGACCAAGA
GAAACGAGAAGTGGTCCGACATGTACGGTTTGATCGTCGCCCAATGGTT
GTCCACCGTCAACACCCAATTCTACACCATCAAGGAGGGTATGTACAAG
GCCTTGAACCTACCAGGCCCAAGCTTTGGAGGAGATCATCAAGTACAGAT
ACAACATCTACTCCGAGAAGGAGAAGTCCAACATTAACATCGACTTCAA
CGACATCAACTCCAAGCTGAACGAGGGTATTAACCAGGCCATCGACAAC
ATCAACAACCTTCATCAACGGTTGTTCCGTCTCCTACTTGATGAAGAAGAT
GATTCCATTGGCCGTCGAGAAGTTGTTGGACTTCGACAACACCCTGAAG
AAGAAGTTGTTGAACCTACATCGACGAGAACAAGTTGTACTTGATCGGTT
CCGCTGAGTACGAGAAGTCCAAGGTCAACAAGTACTTGAAGACCATCAT
GCCATTGACTTGTCCATCTACACCAACGACACCATCTTGATCGAGATGT
TCtaa

B: BoNTB(H_N) encoded protein SEQ ID NO: 22

MAPGICIDVDNEDLFFIADKNSFSDDLKNERIEYNTQSNYIENDFPINELILD
TDLISKIELPSENTESLTDNFNDVPVYEKQPAIKKIFTDENTIFQYLYSQTFPLD
IRDISLTSSFDDALLFSNKVYSFFSMDYIKTANKVVEAGLFAGWVKQIVNDF
VIEANKSNTMDKIADISLIVPYIGLALNVGNETAKGNFENAFEIAGASILFEI
PELLIPVVGAFLLSYIDNKNKIIKTIDNALTKRNEKWSDMYGLIVAQWLST
VNTQFYTIKEGMYKALNYQAQALEEIIKYRYNIYSEKEKSNINIDFNDINSKL
NEGINQAIDNINNFINGCSVSYLMKKMIPLAVEKLLDFDNTLKKNLLNYIDE
NKLYLIGSAEYEKSKVNKYLKTIMPFDL SIYTNDTILIEMF*

FIGURE 13

A: BoNTC₁(H_N) synthetic gene SEQ ID NO: 23

atgTCCCTGTACAACAAGACCCTTGACTGTAGAGAGCTGCTGGTGAAGAA
CACTGACCTGCCATTCATCGGTGACATCAGTGACGTGAAGACTGACATCT
TCCTGCGTAAGGACATCAACGAGGAGACTGAGGTGATCTACTACCCAGA
CAACGTGTCAGTAGACCAAGTGATCCTCAGTAAGAACACCTCCGAGCAT
GGACAAC TAGACCTGCTCTACCCTAGTATCGACAGTGAGAGTGAGATCC
TGCCAGGGGAGAATCAAGTCTTCTACGACAACCGTACCCAGAACGTGGA
CTACCTGAACTCCTACTACTACCTAGAGTCTCAGAAGCTGAGTGACAAC
GTGGAGGACTTCACTTTTACGCGTTCAATCGAGGAGGCTCTGGACAACA
GTGCAAAGGTGTACACTTACTTCCCTACCCTGGCTAACAAGGTGAATGCC
GGTGTGCAAGGTGGTCTGTTCTGATGTGGGCAAACGACGTGGTTGAGG
ACTTCACTACCAACATCCTGCGTAAGGACACACTGGACAAGATCTCAGA
TGTGTCAGCTATCATCCCCTACATCGGACCCGCACTGAACATCTCCAAC
CTGTGCGTCGTGGAACTTCACTGAGGCATTCGCAGTCACTGGTGTCAAC
ATCCTGCTGGAGGCATTCCCTGAGTTCACAATCCCTGCTCTGGGTGCATT
CGTGATCTACAGTAAGGTCCAGGAGCGAAACGAGATCATCAAGACCATC
GACAACGTCTGGAGCAGAGGATCAAGAGATGGAAGGACTCCTACGAGT
GGATGATGGGAACGTGGTTGTCCAGGATCATCACCCAGTTCAACAACAT
CTCCTACCAGATGTACGACTCCCTGAACTACCAGGCAGGTGCAATCAAG
GCTAAGATCGACCTGGAGTACAAGAAGTACTCCGGAAGCGACAAGGAG
AACATCAAGAGCCAGGTTGAGAACCTGAAGAACAGTCTGGACGTCAAG
ATCTCGGAGGCAATGAACAACATCAACAAGTTCATCCGAGAGTGCTCCG
TCACCTACCTGTTCAAGAACATGCTGCCTAAGGTCATCGACGAGCTGAA
CGAGTTCGACCGAAACACCAAGGCAAAGCTGATCAACCTGATCGACTCC
CATAACATCATCCTGGTCGGTGAGGTCGACAAGCTGAAGGCAAAGGTAA
ACAACAGCTTCCAGAAC_{taa}

B: BoNTC₁(H_N) encoded protein SEQ ID NO: 24

MSLYNKTLDCRELLVKNTDLPFIGDISDVKTDIFLRKDINEETEVIYYPDNVS
VDQVILSKNTSEHGQLDLLYPSIDSESEILPGENQVFYDNRTQNVDYLNSYY
YLESQKLSDNVEDFTFTRSIEEALDNSAKVYTYFPTLANKVNAGVQGGLFL
MWANDVVEDFTTNILRKDTLDKISDVSAIIPYIGPALNISNSVRRGNFTEAFA
VTGVTTILLEAFPEFTIPALGAFVIYSKVQERNEIITIDNCLEQRIKRWKDSYE
WMMGTWLSRIITQFNNISYQMYDSLNYQAGAIKAKIDLEYKKYSGSDKENI
KSQVENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNEFDRN
TKAKLINLIDSHNIIIVGEVDKLLKAVNNSFQN*

FIGURE 14

A: BoNTD(H_N) synthetic gene SEQ ID NO: 25

atggccAACTCCCGTGACGACTCCACCTGCATCAAGGTCAAGAACAACAGA
CTGCCATACGTTGCCGACAAGGACTCCATCTCCCAGGAGATCTTCGAGA
ACAAGATCATCACCGACGAGACCAACGTTCAAACTACTCCGACAAGTT
CTCTTTGGACGAGTCCATCCTGGACGGTCAGGTCCCAATCAACCCAGAG
ATCGTCGACCCACTGTTGCCAAACGTCAACATGGAGCCATTGAACTTGCC
AGGTGAGGAGATCGTCTTCTACGACGACATCACCAAGTACGTCGACTAC
TTGAACTCCTACTACTACTTGGAGTCTCAAAAGTTGTCTAACAACGTCGA
GAACATCACCTTGACCACCTCCGTCGAGGAGGCCTTGGGTACTCTAACA
AGATCTACACCTTCCTGCCATCCTTGGCTGAGAAGGTTAACAAGGGTGTT
CAAGCTGGTTTGTTCCTGAACTGGGCCAACGAGGTCGTCGAGGACTTCA
CCACCAACATCATGAAGAAGGACACCCTGGACAAGATCTCCGACGTCTC
CGTCATCATCCCATAACATCGGTCCAGCCTTGAACATCGGTAACCTCCGCCC
TGAGAGGTAACCTCAACCAGGCCTTCGCCACCGCCGGTGTGCGCTTCCTG
CTGGAGGGTTTCCCAGAGTTCACCATCCCAGCCCTGGGTGTCTTCACCTT
CTACTCCTCCATCCAGGAGAGAGAGAAGATCATCAAGACCATCGAGAAC
TGCTTGAGAGCAGAGAGTCAAGAGATGGAAGGACTCCTACCAGTGGATGG
TTTCCAACCTGGCTGTCCAGAATCACCAACCAATTCAACCACATCAACTAC
CAGATGTACGACTCCCTGTCTACCAGGCCGACGCCATCAAGGCCAAGA
TCGACCTGGAGTACAAGAAGTACTCCGGTTCGACAAGGAGAACATCAA
GTCCCAGGTCGAGAACCTGAAGAAGTCTTGGACGTCAAGATCTCCGAG
GCCATGAACAACATCAACAAGTTCATCCGTGAGTGTTCCGTCACCTACCT
GTTCAAGAACATGCTGCCAAAGGTCATCGACGAGCTGAACAAGTTCGAC
CTGAGAACCAAGACCGAGCTGATCAACCTGATCGACTCCCACAACATCA
TCCTGGTTGGTGAGGTTGACtaa

B: BoNTD(H_N) encoded protein SEQ ID NO: 26

MANSRDDSTCIKVKNNRLPYVADKDSISQEIFENKIITDETNVQNYSDKFSLD
ESILDGQVPINPEIVDPLLPNVNMEPLNLPGEIIVFYDDITKYVDYLNSYYYL
ESQKLSNNVENITLTTTSVEEALGYSNKIYTFLPSLAEKVNKG VQAGLFLNWA
NEVVEDFTTNIMKKDTLDKISDVSVIIPYIGPALNIGNSALRGNFNQAFATAG
VAFLEGFPEFTIPALGVFTFYSSIQEREKIIKTIENCLEQRVKRWKDSYQWM
VSNWLSRITTQFNHINYQMYDSL SYQADAIKAKIDLEYKKYSGSDKENIKSQ
VENLKNSLDVKISEAMNNINKFIRECSVTYLFKNMLPKVIDELNKFDLRTKT
ELINLIDSHNIILVGEVD*

FIGURE 15

A: BoNTE(H_N) synthetic gene SEQ ID NO: 27

atgTCCATCTGCATCGAGATCAACAACGGTGAGCTGTTCTTCGTGGCTTCC
GAGAACAGTTACAACGATGACAACATCAACACTCCTAAGGAGATTGACG
ACACCGTCACTTCTAACAACAACACTACGAAAACGACCTGGACCAGGTCAT
CCTAAACTTCAACTCCGAGTCCGCCCTGGTCTGTCCGACGAGAAGCTGA
ACCTGACCATCCAGAACGACGCTTACATCCCAAAGTACGACTCCAACGG
TACATCCGATATCGAGCAGCATGACGTTAACGAGCTTAACGTCTTCTTCT
ACTTAGACGCTCAGAAGGTGCCCGAGGGTGAGAACAAACGTCAATCTCAC
CTCTTCAATTGACACAGCCTTGTTGGAGCAGCCTAAGATCTACACCTTCT
TCTCCTCCGAGTTCATCAACAACGTCAACAAGCCTGTGCAGGCCGCATTG
TTCGTAAGCTGGATTCAGCAGGTGTTAGTAGACTTCACTACTGAGGCTAA
CCAGAAGTCCACTGTTGACAAGATCGCTGACATCTCCATCGTCGTCCCAT
ACATCGGTCTGGCTCTGAACATCGGCAACGAGGCACAGAAGGGCAACTT
CAAGGATGCCCTTGAGTTGTTGGGTGCCGGTATTTTGTGAGTTTGAAC
CCGAGCTGCTGATCCCTACCATCCTGGTCTTCACGATCAAGTCCTTCCTG
GGTTCCTCCGACAACAAGAACAAGGTCATTAAGGCCATCAACAACGCCC
TGAAGGAGCGTGACGAGAAGTGGAAGGAAGTCTATTCTTCATCGTCTC
GAACTGGATGACCAAGATCAACACCCAGTTCAACAAGCGAAAGGAGCA
GATGTACCAGGCTCTGCAGAACCAGGTCAACGCCATCAAGACCATCATC
GAGTCCAAGTACAACCTCCTACACCCTGGAGGAGAAGAACGAGCTTACCA
ACAAGTACGATATCAAGCAGATCGAGAACGAGCTGAACCAGAAGGTCTC
CATCGCCATGAACAACATCGACAGGTTCTGACCGAGTCTCCTCATCTCCT
ACCTGATGAAGCTCATCAACGAGGTCAAGATCAACAAGCTGCGAGAGTA
CGACGAGAATGTCAAGACGTACCTGCTGAACTACATCATCCAGCACGGA
TCCATCCTG_{taa}

B: BoNTE(H_N) encoded protein SEQ ID NO: 28

MSICIEINNGELFFVASSENSYNDDNINTPKEIDDTVTSNNNYENDLDQVILNF
NSESAPGLSDEKLNLTIQNDA YIPKYDSNGTSDIEQHVDNELNVFFYLDAQK
VPEGENNVLNLTSSIDTALLEQPKIYTFSSSEFINNVNKPVQAALFVSWIQQVL
VDFTTEANQKSTVDKIADISIVVPYIGLALNIGNEAQKGNFKDALELLGAGIL
LEFEPELLIPTILVFTIKSFLGSSDNKNKVIKAINNALKERDEKWKEVYSFIVS
NWMTKINTQFNKRKEQMYQALQNQVNAIKTIIESKYNSYTL EEKNELTNKY
DIKQIENELNQKVSIA MNND RFLTESSISYLMKLINEVKINKLREYDENVKT
YLLNYIIQHGSIL*

FIGURE 16

A: BoNTF(H_N) synthetic gene SEQ ID NO: 29

atgGCCCCACCACGTCTGTGTATTAGAGTCAACAACCTCAGAATTATTCTTT
GTCGCTTCCGAGTCAAGCTACAACGAGAACGATATTAACACACCTAAAG
AGATTGACGATACTACCAACCTAAACAACAACCTACCGGAACAACCTTGA
TGAGGTTATTTTGGATTACAACCTCACAGACCATCCCTCAAATTTCCAACC
GTACCTTAAACACTCTTGTCCAAGACAACCTCCTACGTTCCAAGATACGAT
TCTAACGGTACCTCAGAGATCGAGGAGTATGATGTTGTTGACTTTAACGT
CTTTTTCTATTTGCATGCCCAGAAGGTGCCAGAAGGTGAAACCAACATCT
CATTGACTTCTTCCATTGATACCGCCTTGTGGAAGAGTCCAAGGATATC
TTCTTTTCTTCGGAGTTTATCGATACTATCAACAAGCCTGTCAACGCCGC
TCTGTTCAATTGATTGGATTAGCAAGGTCATCAGAGATTTTACCACTGAAG
CTACTCAAAAAGTCCACTGTTGATAAGATTGCTGACATCTCTTTGATTGTC
CCCTATGTCGGTCTTGCTTTGAACATCATTATTGAGGCAGAAAAGGGTAA
CTTTGAGGAGGCTTTTGAATTGTTGGGAGTTGGTATTTTGTGAGTTTG
TTCCAGAACTTACCATTCTGTCAATTTAGTTTTTACGATCAAGTCCTACA
TCGATTCATACGAGAACAAGAATAAAGCAATTAAGCTATTAACAACCTC
CTTGATCGAAAGAGAGGCTAAGTGGAAGGAAATCTACTCATGGATTGTA
TCAAACCTGGCTTACTAGAATTAACACTCAATTTAACAAGAGAAAGGAGC
AAATGTACCAGGCTCTGCAAAACCAAGTCGATGCTATCAAGACTGCAAT
TGAATACAAGTACAACAACATACTTCCGATGAGAAGAACAGACTTGAA
TCTGAATACAATATCAACAACATTGAAGAAGAGTTGAACAAGAAAGTTT
CTTTGGCTATGAAGAATATCGAAAGATTTATGACCGAATCCTCTATCTCT
TACTTGATGAAGTTGATCAATGAGGCCAAGGTTGGTAAGTTGAAGAAGT
ACGATAACCACGTTAAGAGCGATCTGCTGAACTACATTCTCGACCACAG
ATCAATCCTGGGAGAGCAGACAAACGAGCTGAGTGATTGGTTACTTCC
ACTTTGAACTCCTCCATTCCATTTGAGCTTTCT_{taa}

B: BoNTF(H_N) encoded protein SEQ ID NO: 30

MAPPRLCIRVNNSELFFVASESSYNENDINTPKEIDDTNLNNNYRNNLDEVI
LDYNSQTIPQISNRTLNLVQDNSYVPRYDSNGTSEIEEYDVVDNFVFFYLH
AQKVPEGETNISLTSSIDTALLEESKDIFFSSEFIDTINKPVNAALFIDWISKVIR
DFTTEATQKSTVDKIADISLIVPYVGLALNIIIEAEKGNFEEAFELLGVGILLEF
VPELTIPVILVFTIKSYIDSYENKNKAIKAINNSLIEREAKWKEIYSWIVSNWL
TRINTQFNKRKEQMYQALQNQVDAIKTAIEYKYNNTSDEKNRLESEYNIN
NIEEELNKKVSLAMKNIERFMTESISYLMKLINEAKVGKLKKYDNHVKS
LDLNYILDHRSILGEQTNELSDLVTSTLNSSIPFELS*

FIGURE 17

A: BoNTG(H_N) synthetic gene SEQ ID NO: 31

atggccAAAAATACCGGTAAATCTGAACAGTGTATTATTGTTAATAATGAG
GATTTATTTTTTCATAGCTAATAAAGATAGTTTTTCAAAGATTTAGCTAA
AGCAGAACTATAGCATATAATACACAAAATAATACTATAGAAAATAAT
TTTTCTATAGATCAGTTGATTTTAGATAATGATTTAAGCAGTGGCATAGA
CTTACCAAATGAAAACACAGAACCATTACAAATTTTGACGACATAGAT
ATCCCTGTGTATATTAAACAATCTGCTTTAAAAAAAATTTTGTGGATGG
AGATAGCCTTTTTGAATATTTACATGCTCAAACATTTCCCTTCTAATATAG
AAAATCTACAATAACGAATTCATTAAATGATGCTTTAAGAAATAATAA
TAAAGTCTATACTTTTTTTCTACAAACCTTGTTGAAAAAGCTAATACAG
TTGTAGGTGCTTCACCTTTTGTAACTGGGTAAAAGGAGTAATAGATGAT
TTTACATCTGAATCCACACAAAAAAGTACTATAGATAAAGTTTCAGATGT
ATCCATAATTATCCCTATATAGGACCTGCTTTGAATGTAGGAAATGAAA
CAGCTAAAGAAAATTTTAAAAATGCTTTTGAATAGGTGGAGCCGCTAT
CTTAATGGAGTTTATTCCAGAATTATTGTACCTATAGTTGGATTTTTTAC
ATTAGAATCATATGTAGGAAATAAAGGGCATATTATTATGACGATATCC
AATGCTTTAAAGAAAAGGGATCAAAAATGGACAGATATGTATGGTTTGA
TAGTATCGCAGTGGCTCTCAACGGTTAACTCAATTTTATACAATAAAA
GAAAGAATGTACAATGCTTTAAATAATCAATCACAAGCAATAGAAAAAA
TAATAGAAGATCAATATAATAGATATAGTGAAGAAGATAAAATGAATAT
TAACATTGATTTTAAATGATATAGATTTTAAACTTAATCAAAGTATAAATT
TAGCAATAAACAATATAGATGATTTTATAAACCAATGTTCTATATCATAT
CTAATGAATAGAATGATTCATTAGCTGTAAAAAAGTTAAAAGACTTTG
ATGATAATCTTAAGAGAGATTTATTGGAGTATATAGATACAAATGAAC
ATATTTACTTGATGAAGTAAATATTCTAAAATCAAAGTAAATAGACAC
CTAAAAGACAGTATACCATTTGATCTTTCCTATATACCTaa

B: BoNTG(H_N) encoded protein SEQ ID NO: 32

MAKNTGKSEQCHVNNEDLFFIANKDSFSKDLAKAETIAYNTQNNTIENNFSI
DQLILDNDLSSGIDLPNENTEPFTNFDDIDIPVYIKQSALKKIFVDGDSLFEYL
HAQTFPSNIENLQLTNSLNDALRNNNKVYTFSTNLVEKANTVVGASLFVN
WVKGVIDDFTSESTQKSTIDKVSDVSIIPYIGPALNVGNETAKENFKNAFEIG
GAAILMEFIPELIVPIVGFFTLESYVGNKGHIIMTISNALKKRDQKWTDMYGL
IVSQWLSTVNTQFYTIKERMYNALNNQSQAIEKIIEDQYNRYSEEDKMNINI
DFNDIDFKLNQSINLAINNIDDFINQCSISYLMNRMIPLAVKKLKDFDDNLKR
DLLEYIDTNELYLLDEVNLIKSKVNRHLKDSIPFDLSLYT*

FIGURE 18

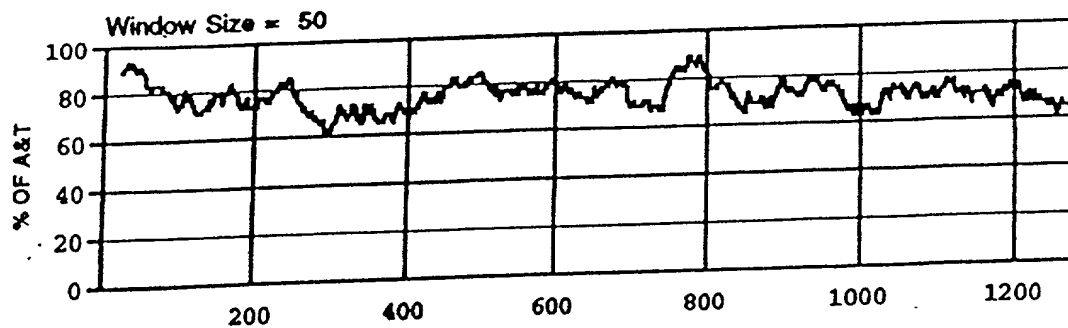
A: First BoNTF(Hc) gene: SEQ ID NO: 33

GAATTCACGatgTCTTACACTAACGACAAAATCCTGATCCTGTACTTCAAC
AAACTGTACAAAAAATCAAAGACAACCTCTATCCTGGACATGCGTTACG
AAAACAACAAATTCATCGACATCTCTGGCTATGGTTCTAACATCTCTATC
AACGGTGACGTCTACATCTACTCTACTAACCGCAACCAGTTCGGTATCTA
CTCTTCTAAACCGTCTGAAGTAAACATCGCTCAGAACAACGACATCATCT
ACAACGGTTCGTTACCAGAACTTCTCTATCTCTTTCTGGGTTTCGTATCCCG
AAATACTTCAACAAAGTTAACCTGAACAACGAATACACTATCATCGACT
GCATCCGTAACAACAACCTCTGGTTGGAAAATCTCTCTGAACTACAACAA
AATCATCTGGACTCTGCAGGACACTGCTGGTAACAACCAGAACTGGTT
TTCAACTACACTCAGATGATCTCTATCTCTGACTACATTAATAAATGGAT
CTTCGTTACTATCACTAACAACCGTCTGGGTAACCTCTCGTATCTACATCA
ACGGTAACCTGATCGATGAAAAATCTATCTCTAACCTGGGTGACATCCA
CGTTTCTGACAACATCCTGTTCAAATCGTTGGTTGCAACGACACGCGTT
ACGTTGGTATCCGTTACTTCAAAGTTTTCGACACTGAACTGGGTAAAACT
GAAATCGAACTCTGTACTCTGACGAACCGGACCCGTCTATCCTGAAAG
ACTTCTGGGGTAACTACCTGCTGTACAACAACGTTACTACCTGCTGAAC
CTGCTCCGGACTGACAAATCTATCACTCAGAACTCTAACTTCCTGAACAT
CAACCAGCAGCGTGGTGTATATCAGAAACCTAATATCTTCTCTAACTC
GTCTGTACACTGGTGTGAAGTTATCATCCGTAAAAACGGTTCTACTGAC
ATCTCTAACTGACAACTTCGTACGTAAAAACGACCTGGCTTACATCAA
CGTTGTTGACCGTGACGTTGAATACCGTCTGTACGCTGACATCTCTATCG
CTAAACCGGAAAAAATCATCAAACCTGATCCGTACTTCTAACTCTAACAA
CTCTCTGGGTCAGATCATCGTTATGGACTCGATCGGTAACAACCTGCACTA
TGAACCTCCAGAACAAACAACGGTGGTAACATCGGTCTGCTGGGTTTCCA
CTCTAACAACTGGTTGCTTCTTCATGGTACTACAACAACATCCGTAAAA
ACACTTCTTCTAACGGTTGCTTCTGGTCTTTCATCTCTAAAGAACACGGTT
GGCAGGAAAACTaaGAATTC

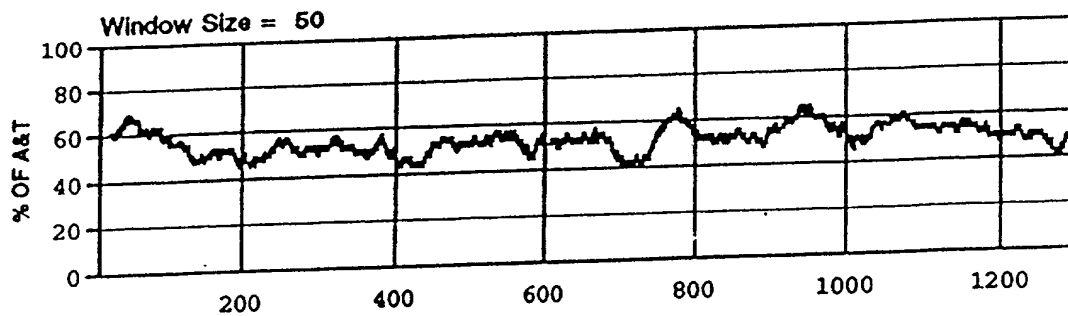
B: BoNTF(Hc) #1 encoded protein: SEQ ID NO: 34

MSYTNDKILILYFNKLYKKIKDNSILDMRYENNKFIDISGYGSNISINGDVYIY
STNRNQFGIYSSKPSEVNIAQNNDIYNGRYQNFSISFWVRIPKYFNKVNLLN
EYTIIDCIRNNNSGWKISLNYNKIIWTLQDTAGNNQKLVFNQTQMISISDYIN
KWIFVTITNNRLGNSRIYINGNLIDEKSISNLGDIHVSDNILFKIVGCNDTRYV
GIRYFKVFDTELKGTEIETLYSDEPDPSILKDFWGNLYLLYNKRYLLNLLRT
DKSITQNSNFLNINQQRGVYQKPNIFSNTRLYTGVEVIIRKNGSTDISNTDNF
VRKNDLAYINVVDRDVEYRLYADISIAKPEKIIKLIRTSNSNNSLGQIIVMSI
GNNCTMNFQNNNGGNIGLLGFHSNNLVASSWYNNIRKNTSSNGCFWSFIS
KEHGWQEN*

A: Natural BoNTF(Hc) Gene



B: First BoNTF(Hc) Synthetic Gene



C: Second BoNTF(Hc) Synthetic Gene

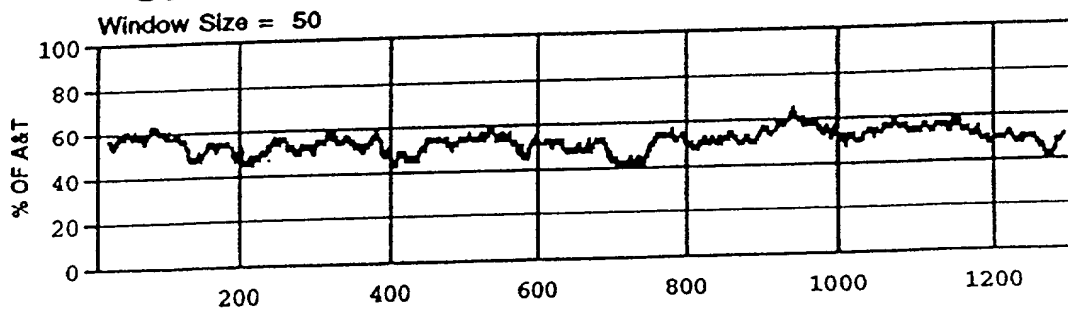
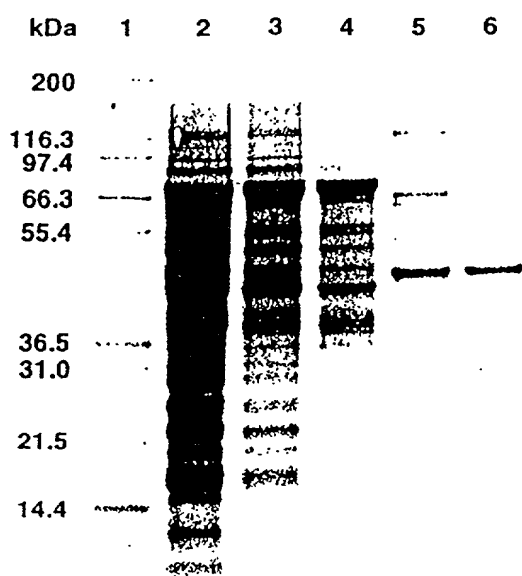


Fig 19

A



B

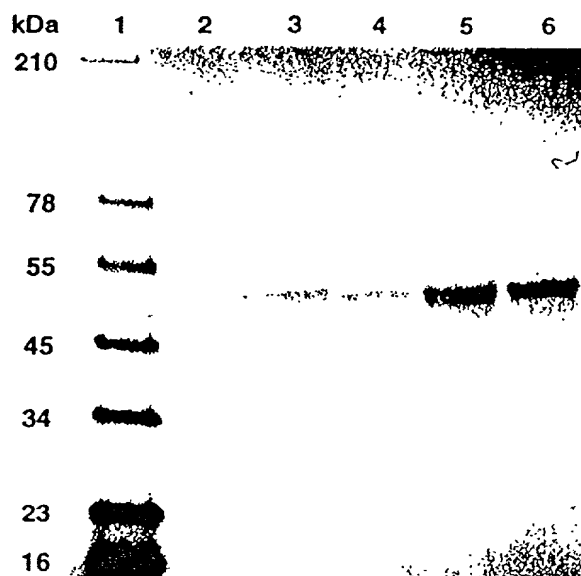


Fig 20

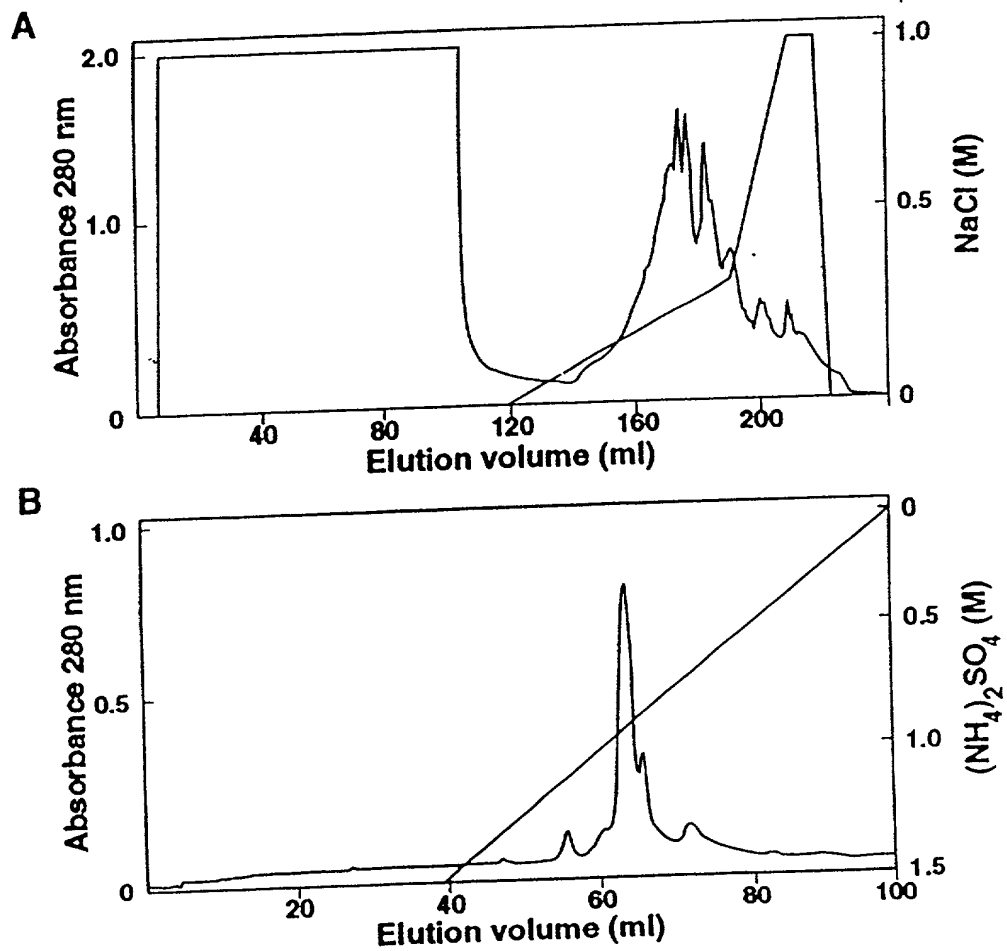


Fig 21

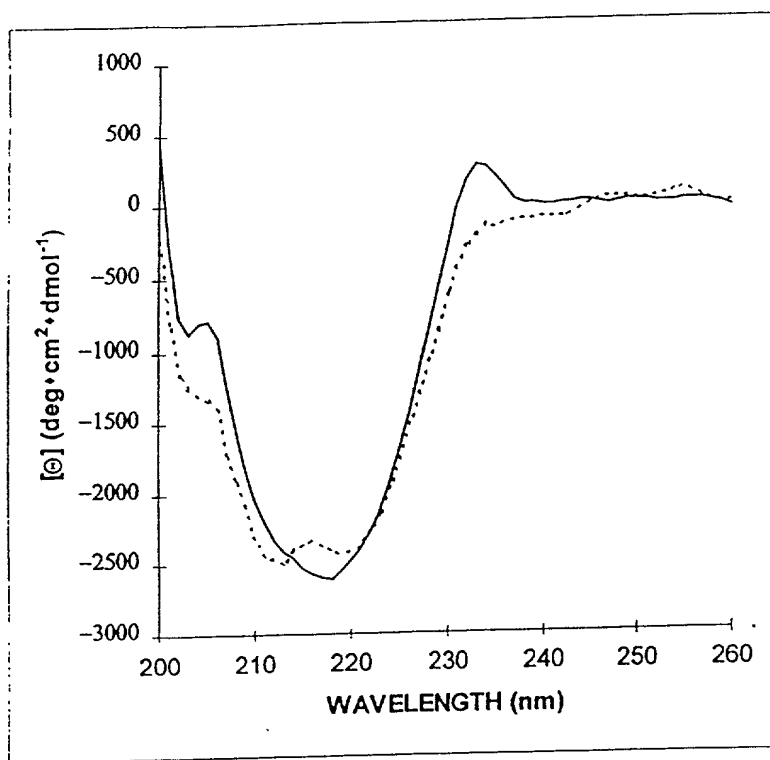


Fig 22